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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/557,992	01/09/2006	Yoshio Umezawa	2005_1843A	7824

513 7590 07/08/2008

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EXAMINER	
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ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
07/08/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/557,992	UMEZAWA ET AL.	
	Examiner	Art Unit	
	Rebecca E. Prouty	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *6-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 November 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group I, Claims 1-5 drawn to a pair of probes for analyzing protein-protein interactions, which comprises a probe containing at least an N-terminal half polypeptide of split *Renilla* luciferase and a probe containing at least the remaining C-terminal half polypeptide of split *Renilla* luciferase in the reply filed on 3/25/08 is acknowledged.

Claims 6-10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/25/08.

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the specification. It is particularly noted that Figures 3 recites sequences but neither the figure nor the brief description of the drawing recites the corresponding sequence identifier. See particularly 37 CFR 1.821(d).

Claim 2 is objected to because of the following informalities: "N-split *Renilla* luciferase" should be "the N-terminal half of split *Renilla* luciferase" and "C-split *Renilla* luciferase" should be "the C-terminal half of split *Renilla* luciferase". Appropriate correction is required.

Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the presence in each of probe A and probe B of one of two proteins which are to be tested for their ability to interact. These are essential elements of the claims as without their presence fragments of *Renilla* luciferase are not probes for analyzing protein-protein interactions. Furthermore, claim 3 should make it clear that the linkers of probes A and B are situated between the fragments of the *Renilla* luciferase and the proteins to be tested for interaction.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "Ser91" and "Tyr92" in claim 5 is unclear and confusing absent reference to a specific amino acid sequence. It is suggested that "obtained by splitting *Renilla* luciferase between Ser91 and Tyr92" be amended "obtained by splitting the *Renilla* luciferase of SEQ ID NO:1 between Ser91 and Tyr92".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Paulmurugan et al.

Paulmurgan et al. teach several pairs of split *Renilla* luciferase fragments in which the N-terminal portion of the luciferase is fused through a 10 amino acid long linker to the Id protein and the C-terminal portion of the luciferase is fused through a 10 amino acid long linker to the MyoD protein and use of these pairs for assaying the interaction of the MyoD and Id proteins.

Claims 1, 3, 4 and 5 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaihara et al. (Reference AO of applicants IDS).

Kaihara et al. teach several pairs of split *Renilla* luciferase fragments in which the N-terminal portion of the luciferase is fused through a 13 amino acid long linker to the insulin-receptor substrate (IRS) 1 peptide and the C-terminal portion of the luciferase is fused through a 13 amino acid long

linker to the p85 SH2 domain and use of these pairs for assaying the interaction of the IRS-1 peptide and p85 SH2 domain. The protein pair of Kaihara et al. include split *Renilla* luciferase fragments in which the *Renilla* luciferase is split between Ser91 and Tyr92.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Paulmurgan et al. or Kaihara et al. (Reference AO of applicants IDS) in view of Umezawa et al. (US-PGPUBS 2003/0003506).

Paulmurgan et al. and Kaihara et al. are both discussed above and each teach pairs of split *Renilla* luciferase fragments

fused to a pair of proteins through a linker for measuring the interaction of the fused proteins. Neither of the references disclose the inclusion of a split intein in each probe wherein the interaction of the protein pair results in the reconstitution of an active intein which catalyzes its own removal and recreation of the full length *Renilla* luciferase.

Umezawa et al. teach a variation on standard split-enzyme (and in particular a split luciferase) protein-protein interaction assay systems in which the two fusion proteins used are modified to include an N-terminal fragment of an intein fused to the C-terminal end of the N-terminal fragment of the split enzyme and a C-terminal fragment of an intein is fused to the N-terminus of the C-terminal fragment of the split enzyme in wherein the interaction of the proteins fuse to the split-protein fragments brings the N-terminal and C-terminal fragments of the intein into sufficient proximity to reconstitute an active intein which then catalyzes its own splicing out of the complex and the formation of a peptide bond between the C-terminal end of the N-terminal fragment of the split enzyme and the N-terminal end of the C-terminal fragment of the split enzyme thus recreating the full length enzyme. This system has the advantage of actually recreating the reporter enzyme as a single polypeptide chain upon interaction of the proteins

instead to merely allowing them to associate non-covalently to recreate the active reporter thus increasing the accuracy and sensitivity of the assay. Umezawa et al.'s system used firefly luciferase fragments as the split reporter but did not disclose use of *Renilla* luciferase fragments.

Therefore it would have been obvious to one of ordinary skill in the art to modify the split *Renilla* luciferase fragments of either of Paulmurgan et al. or Kaihara et al. to include split intein fragments as taught by Umezawa et al. in order that the system recreate the *Renilla* luciferase as a single polypeptide chain upon interaction of the proteins instead of merely allowing them to associate non-covalently to recreate the active reporter and increase the accuracy and sensitivity of the assay.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 of copending Application No. 10/591,990. Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-4 herein and claims 1-4 of copending application 10/591,990 are both directed to a pair of probes for analyzing protein-protein interactions in which probe A contains an N-terminal fragment of a reporter polypeptide and an N-terminal half of an intein and probe B contains an C-terminal fragment of a reporter polypeptide and an C-terminal half of an intein The claims differ in that the claims of the instant application specifically recite that the reporter polypeptide is *Renilla* luciferase while the claims of the copending application recite that one of the two probes includes a nuclear localization signal (NLS). However, the presence of a NLS is not excluded

from the instant claims. The portion of the specification in 10/591,990 that supports the recited reporter polypeptide includes an embodiment that would anticipate claims 1-2 herein, e.g., the reporter polypeptide is *Renilla* luciferase (see page 14). Claims 1-2 herein cannot be considered patentably distinct over claims 1-4 of 10/591,990 when there is a specifically recited embodiment (the reporter polypeptide is *Renilla* luciferase) that would anticipate claims 1 and 2. Alternatively, claims 1-2 herein cannot be considered patentably distinct over claims 1-4 of 10/591,990 when there is a specifically disclosed embodiment in 10/591,990 that supports claims 1-4 of that application and falls within the scope of claims 1-2 herein because it would have been obvious to one having ordinary skill in the art to modify the probes of claims 1-4 of the copending application by selecting a specifically disclosed embodiment that supports that claim, i.e., the reporter polypeptide is *Renilla* luciferase. One having ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims 1-4. Furthermore, while the claims of the copending application do not specifically recite a linker as recited in instant claims 3-4, the use of a linker of 3-20 amino acids between the domains of split-enzyme probes such as those

of claims 1-4 of copending application 10/591,990 was well known in the art to provide sufficient flexibility and separation of the fused domains and thus the further inclusion of a liner would have been obvious to one of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rebecca E. Prouty whose telephone number is 571-272-0937. The examiner can normally be reached on Tuesday-Friday from 8 AM to 5 PM. The examiner can also be reached on alternate Mondays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed, can be reached at (571) 272-0934. The fax phone number for this Group is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rebecca Prouty/
Primary Examiner
Art Unit 1652